at page 28, line 8, replace "map of a conjugate MCP-3-AM-Shiga-A1" with —map of a plasmid, designated pOPL101, encoding the conjugate MCP-3-AM-Shiga-A1—.

REMARKS

This response is supplemental to the Amendment, mailed September 5, 2000 and provides the Declaration noted therein. The Amendment and remarks therein, mailed on September 5, 2000, is incorporated herein in its entirety. Any fees that may be due in connection with this paper or with this application may be charged to Deposit Account No. 50-1213. If a Petition for extension of time is needed, this paper is to be considered such Petition.

Claims 26-29, 31, 32, 35-38, 40, 42, 44-46, 48-54, 57 and 65-87 are presently pending in this application.

The DECLARATION is provided to cull evidence from the specification and to provide data that rebut the assertions made by the Office in setting forth the rejection under 35 U.S.C. §112, first paragraph, and also to show results that are not taught or suggested by the cited art.

THE DECLARATION

The DECLARATION, although not necessary to demonstrate enablement, is provided to supplement the remarks in the previous response. Much of the discussion and some of the data in the DECLARATION is also in the application.

1) It is urged that the specification provides no guidance of how to treat "every possible disorder associated with an inflammatory response."

2) It is alleged that it is "not predictable to one of skill in the art how to use a method of treating a patient with 'any' type of inflammatory response", because "Applicants do not give exact dosages or a treatment regimen."

3) Further, it is alleged that no guidance is provided, or working examples, for use of the claimed compounds in treating patients who have a disorder of the immune system, and it is not predictable to one of ordinary skill

in the art how to treat such disorders without causing further disorders to the altered immune system.

The DECLARATION provides data that shows that the chemokine receptor targeting agent conjugates specifically target activated proliferating or migrating cells, and not quiescent cells. The DECLARATION also provides data showing that conjugates specifically target cells that express receptors to which the chemokine targeting agent binds. The DECLARATION also provides data from a mouse xenograft model showing low toxicity, in fact lower than expected, and specific targeting of tumor cells.

The DECLARATION describes explains that by targeting chemokine receptors, the conjugates are not being used to treat all or any inflammatory diseases, but to treat the inflammatory response or proliferative that accompanies or causes many disease states. Because there many chemokines and many receptors therefor and because only certain chemokine receptors are upregulated in particular conditions, it is possible to specifically and selectively target the proliferating and migrating cells that are responsible for the pathophysiological response. This type of response is shared by many diseases, including CNS trauma, arthritis, asthma, cancer cell proliferation and others (at least seventy are discussed in the specification), and particular chemokine receptors are upregulated on cells that are responsible for the disease. As taught in the specification and discussed in the DECLARATION, it is possible to select chemokine receptor targeting agents to target a particular population of cells that is proliferating or migrating in the disease state and to thereby inhibit the progression or possibly eliminate the disease. In fact, as described, it will be possible to administer a series or a combination of the conjugate to specifically target the cells that are proliferating and migrating as a disease progresses.

The DECLARATION also describes how the skilled artisan can select the appropriate targeting agent for treatment of a selected disease and how the skilled artisan can select appropriate dosages. This material is also included in

the specification. The DECLARATION also provide evidence that immunosuppression is not an issue with these conjugates because they specifically target activated cells.

By showing the exquisite selectivity of the conjugates provided in this application, the DECLARATION also shows results not taught or suggested by the cited references, which do not mention the use of chemokine receptor-targeting agents.

* * *

In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
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